Blast 2 Sequences results

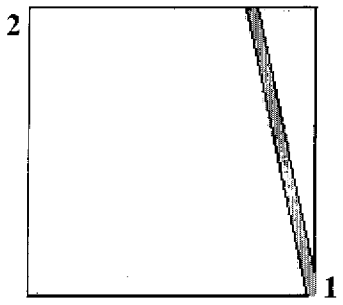
PubMed Entrez BLAST OMIM Taxonomy Structure

BLAST 2 SEQUENCES RESULTS VERSION BLASTN 2.2.17 [Aug-26-2007]

Match: 1 Mismatch: -2 gap open: 5 gap extension: 2
x_dropoff: 0 expect: 10.000(wordsize: 11 Filter ☑ View option Standard
Masking character option X for protein, n for nucleotide Masking color option Black
☐ Show CDS translation Align

Sequence 1: gi|37181733|Homo sapiens clone DNA58721 NAG14 (UNQ554) mRNA, complete cds
Length = 2185 (1 .. 2185)

Sequence 2: gi|5236323|wj26h10.x1 NCI_CGAP_Kid12 Homo sapiens cDNA clone IMAGE:2404003 3', mRNA sequence.
Length = 478 (1 .. 478)



NOTE:Bitscore and expect value are calculated based on the size of the nr database.

NOTE:If protein translation is reversed, please repeat the search with reverse strand of the query sequence.

```
 Score =  888 bits (462),  Expect = 0.0
 Identities = 478/478 (100%), Gaps = 0/478 (0%)
 Strand=Plus/Minus

Query  1703  ACTTCGTAAGCGGCACCAGCAGCGGAGTACAGTCACAGCCGCCCGGACTGTTGAGATAAT  1762
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  478   ACTTCGTAAGCGGCACCAGCAGCGGAGTACAGTCACAGCCGCCCGGACTGTTGAGATAAT  419

Query  1763  CCAGGTGGACGAAGACATCCCAGCAGCAACATCCGCAGCAGCAACAGCAGCTCCGTCCGG  1822
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  418   CCAGGTGGACGAAGACATCCCAGCAGCAACATCCGCAGCAGCAACAGCAGCTCCGTCCGG  359

Query  1823  TGTATCAGGTGAGGGGGCAGTAGTGCTGCCCACAATTCATGACCATATTAACTACAACAC  1882
```

```
Sbjct  358   TGTATCAGGTGAGGGGGCAGTAGTGCTGCCCACAATTCATGACCATATTAACTACAACAC  299

Query  1883  CTACAAACCAGCACATGGGGCCCACTGGACAGAAAACAGCCTGGGGAACTCTCTGCACCC  1942
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  298   CTACAAACCAGCACATGGGGCCCACTGGACAGAAAACAGCCTGGGGAACTCTCTGCACCC  239

Query  1943  CACAGTCACCACTATCTCTGAACCTTATATAATTCAGACCCATACCAAGGACAAGGTACA  2002
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  238   CACAGTCACCACTATCTCTGAACCTTATATAATTCAGACCCATACCAAGGACAAGGTACA  179

Query  2003  GGAAACTCAAATATGACTCCCCTCCCCCAAAAAACTTATAAAATGCAATAGAATGCACAC  2062
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  178   GGAAACTCAAATATGACTCCCCTCCCCCAAAAAACTTATAAAATGCAATAGAATGCACAC  119

Query  2063  AAAGACAGCAACTTTTGTACAGAGTGGGGAGAGACTTTTTCTTGTATATGCTTATATATT  2122
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  118   AAAGACAGCAACTTTTGTACAGAGTGGGGAGAGACTTTTTCTTGTATATGCTTATATATT  59

Query  2123  AAGTCTATGGGCTGGTTAAAAAAAACAGATTATATTAAAATTTAAAGACAAAAAGTCA  2180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  58    AAGTCTATGGGCTGGTTAAAAAAAACAGATTATATTAAAATTTAAAGACAAAAAGTCA  1
```

CPU time: 0.11 user secs. 0.03 sys. secs 0.14 total secs.

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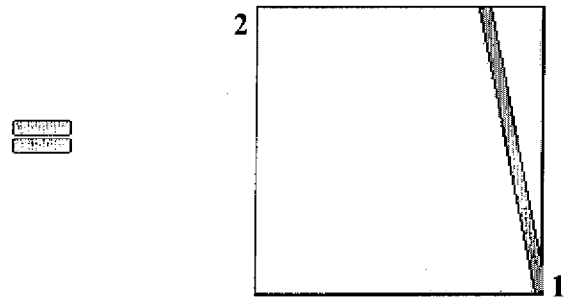
BLAST 2 SEQUENCES RESULTS VERSION BLASTN 2.2.17 [Aug-26-2007]

Match: 1 Mismatch: -2 gap open: 5 gap extension: 2
x_dropoff: 0 expect: 10.0000 wordsize: 11 Filter ☑ View option Standard
Masking character option X for protein, n for nucleotide Masking color option Black
☐ Show CDS translation Align

Sequence 1: gi|37181733|Homo sapiens clone DNA58721 NAG14 (UNQ554) mRNA, complete cds
Length = 2185 (1 .. 2185)

Sequence 2: gi|4302966|th94b04.x1 Soares_NSF_F8_9W_OT_PA_P_S1 Homo sapiens cDNA clone IMAGE:2126287 3', mRNA sequence.
Length = 447 (1 .. 447)



NOTE: Bitscore and expect value are calculated based on the size of the nr database.

NOTE: If protein translation is reversed, please repeat the search with reverse strand of the query sequence.

```
 Score =  817 bits (425),  Expect = 0.0
 Identities = 441/441 (100%), Gaps = 0/441 (0%)
 Strand=Plus/Minus

Query  1743  GCCCGGACTGTTGAGATAATCCAGGTGGACGAAGACATCCCAGCAGCAACATCCGCAGCA  1802
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  447   GCCCGGACTGTTGAGATAATCCAGGTGGACGAAGACATCCCAGCAGCAACATCCGCAGCA  388

Query  1803  GCAACAGCAGCTCCGTCCGGTGTATCAGGTGAGGGGGCAGTAGTGCTGCCCACAATTCAT  1862
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  387   GCAACAGCAGCTCCGTCCGGTGTATCAGGTGAGGGGGCAGTAGTGCTGCCCACAATTCAT  328

Query  1863  GACCATATTAACTACAACACCTACAAACCAGCACATGGGGCCCACTGGACAGAAAACAGC  1922
```

```
Sbjct  327   GACCATATTAACTACAACACCTACAAACCAGCACATGGGGCCCACTGGACAGAAAACAGC  268

Query  1923  CTGGGGAACTCTCTGCACCCCACAGTCACCACTATCTCTGAACCTTATATAATTCAGACC  1982
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  267   CTGGGGAACTCTCTGCACCCCACAGTCACCACTATCTCTGAACCTTATATAATTCAGACC  208

Query  1983  CATACCAAGGACAAGGTACAGGAAACTCAAATATGACTCCCCTCCCCCAAAAAACTTATA  2042
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  207   CATACCAAGGACAAGGTACAGGAAACTCAAATATGACTCCCCTCCCCCAAAAAACTTATA  148

Query  2043  AAATGCAATAGAATGCACACAAAGACAGCAACTTTTGTACAGAGTGGGGAGAGACTTTTT  2102
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  147   AAATGCAATAGAATGCACACAAAGACAGCAACTTTTGTACAGAGTGGGGAGAGACTTTTT  88

Query  2103  CTTGTATATGCTTATATATTAAGTCTATGGGCTGGTTAAAAAAAACAGATTATATTAAAA  2162
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  87    CTTGTATATGCTTATATATTAAGTCTATGGGCTGGTTAAAAAAAACAGATTATATTAAAA  28

Query  2163  TTTAAAGACAAAAAGTCAAAA  2183
              ||||||||||||||||||||
Sbjct  27    TTTAAAGACAAAAAGTCAAAA  7
```

CPU time: 0.10 user secs. 0.05 sys. secs 0.15 total secs.

Blast 2 Sequences results

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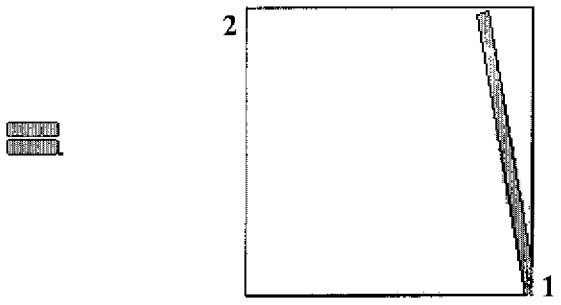
BLAST 2 SEQUENCES RESULTS VERSION BLASTN 2.2.17 [Aug-26-2007]

Match: 1 Mismatch: -2 gap open: 5 gap extension: 2
x_dropoff: 0 expect: 10.000(wordsize: 11 Filter ☑ View option Standard
Masking character option X for protein, n for nucleotide Masking color option Black
☐ Show CDS translation Align

Sequence 1: gi|37181733|Homo sapiens clone DNA58721 NAG14 (UNQ554) mRNA, complete cds
Length = 2185 (1 .. 2185)

Sequence 2: gi|4333021|ti91c05.x1 NCI_CGAP_Kid11 Homo sapiens cDNA clone IMAGE:2139368 3', mRNA sequence.
Length = 393 (1 .. 393)



NOTE:Bitscore and expect value are calculated based on the size of the nr database.

NOTE:If protein translation is reversed, please repeat the search with reverse strand of the query sequence.

```
 Score =  710 bits (369),  Expect = 0.0
 Identities = 385/385 (100%), Gaps = 0/385 (0%)
 Strand=Plus/Minus

Query  1795  CCGCAGCAGCAACAGCAGCTCCGTCCGGTGTATCAGGTGAGGGGGCAGTAGTGCTGCCCA  1854
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  385   CCGCAGCAGCAACAGCAGCTCCGTCCGGTGTATCAGGTGAGGGGGCAGTAGTGCTGCCCA  326

Query  1855  CAATTCATGACCATATTAACTACAACACCTACAAACCAGCACATGGGGCCCACTGGACAG  1914
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  325   CAATTCATGACCATATTAACTACAACACCTACAAACCAGCACATGGGGCCCACTGGACAG  266

Query  1915  AAAACAGCCTGGGGAACTCTCTGCACCCCACAGTCACCACTATCTCTGAACCTTATATAA  1974
```

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                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  265   AAAACAGCCTGGGGAACTCTCTGCACCCCACAGTCACCACTATCTCTGAACCTTATATAA  206

Query  1975  TTCAGACCCATACCAAGGACAAGGTACAGGAAACTCAAATATGACTCCCCTCCCCCAAAA  2034
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  205   TTCAGACCCATACCAAGGACAAGGTACAGGAAACTCAAATATGACTCCCCTCCCCCAAAA  146

Query  2035  AACTTATAAAATGCAATAGAATGCACACAAAGACAGCAACTTTTGTACAGAGTGGGGAGA  2094
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  145   AACTTATAAAATGCAATAGAATGCACACAAAGACAGCAACTTTTGTACAGAGTGGGGAGA  86

Query  2095  GACTTTTTCTTGTATATGCTTATATATTAAGTCTATGGGCTGGTTAAAAAAAACAGATTA  2154
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  85    GACTTTTTCTTGTATATGCTTATATATTAAGTCTATGGGCTGGTTAAAAAAAACAGATTA  26

Query  2155  TATTAAAATTTAAAGACAAAAAGTC  2179
              |||||||||||||||||||||||||
Sbjct  25    TATTAAAATTTAAAGACAAAAAGTC  1
```

CPU time: 0.11 user secs. 0.04 sys. secs 0.15 total secs.

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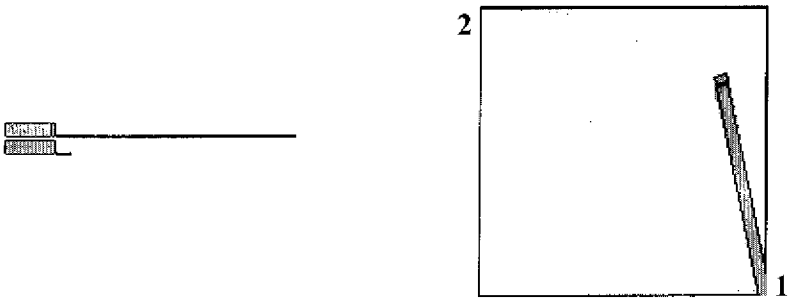
BLAST 2 SEQUENCES RESULTS VERSION BLASTN 2.2.17 [Aug-26-2007]

Match: 1 Mismatch: -2 gap open: 5 gap extension: 2
x_dropoff: 0 expect: 10.0000 wordsize: 11 Filter ☑ View option Standard
Masking character option X for protein, n for nucleotide Masking color option Black
☐ Show CDS translation Align

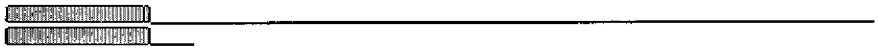
Sequence 1: gi|37181733|Homo sapiens clone DNA58721 NAG14 (UNQ554) mRNA, complete cds
Length = 2185 (1 .. 2185)

Sequence 2: gi|517914|IB1836 Infant brain, Bento Soares Homo sapiens cDNA 3'end, mRNA sequence.
Length = 470 (1 .. 470)



NOTE:Bitscore and expect value are calculated based on the size of the nr database.

NOTE:If protein translation is reversed, please repeat the search with reverse strand of the query sequence.



```
Score =  619 bits (322),  Expect = 1e-173
Identities = 353/359 (98%), Gaps = 2/359 (0%)
Strand=Plus/Minus

Query  1828  CAGGTGAGGGGGC--AGTAGTGCTGCCCACAATTCATGACCATATTAACTACAACACCTA  1885
              ||||||||||||    ||||||||||||||||||||||||||| |||||||||||  ||||
Sbjct  359   CAGGTGAGGGGGGCAAGTAGTGCTGCCCACAATTCATGACCATTTTAACTACAACNCCTA  300

Query  1886  CAAACCAGCACATGGGGCCCACTGGACAGAAAACAGCCTGGGGAACTCTCTGCACCCCAC  1945
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  299   CAAACCAGCACATGGGGCCCACTGGACAGAAAACAGCCTGGGGAACTCTCTGCACCCCAC  240

Query  1946  AGTCACCACTATCTCTGAACCTTATATAATTCAGACCCATACCAAGGACAAGGTACAGGA  2005
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
```

```
Sbjct  239   AGTCACCACTATCTCTGAACCTTATATAATTCAGACCCATACCAAGGACAAGGTACAGGA  180

Query  2006  AACTCAAATATGACTCCCCTCCCCCAAAAAACTTATAAAATGCAATAGAATGCACACAAA  2065
              ||||||||||||||||||||||||||||||||| ||||||||||||||||||||||||
Sbjct  179   AACTCAAATATGACTCCCCTCCCCCAAAAAACTTATNAAATGCAATAGAATGCACACAAA  120

Query  2066  GACAGCAACTTTTGTACAGAGTGGGGAGAGACTTTTTCTTGTATATGCTTATATATTAAG  2125
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  119   GACAGCAACTTTTGTACAGAGTGGGGAGAGACTTTTTCTTGTATATGCTTATATATTAAG  60

Query  2126  TCTATGGGCTGGTTAAAAAAAACAGATTATATTAAAATTTAAAGACAAAAAGTCAAAAC  2184
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  59    TCTATGGGCTGGTTAAAAAAAACAGATTATATTAAAATTTAAAGACAAAAAGTCAAAAC  1
```

CPU time: 0.10 user secs. 0.05 sys. secs 0.15 total secs.

glycosylation sites from about amino acid 138 to about amino acid 141 and from about amino acid 361 to about amino acid 364. Clone DNA59820-1549 has been deposited with the ATCC on August 18, 1998 and is assigned ATCC deposit no. 203129.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using the ALIGN-2 sequence alignment analysis of the full-length sequence shown in Figure 44 (SEQ ID NO:57) evidenced sequence identity between the PRO1281 amino acid sequence and the following Dayhoff sequences: S44860, CET24D1_1, CEC38H2_3, CAC2_HAECO, B3A2_HUMAN, S22373, CEF38A3_2, CEC34F6_2, CEC34F6_3 and CELT22B11_3.

EXAMPLE 23

Gene Amplification

This example shows that the PRO212-, PRO290-, PRO341-, PRO535-, PRO619-, PRO717-, PRO809-, PRO830-, PRO848-, PRO943-, PRO1005-, PRO1009-, PRO1025-, PRO1030-, PRO1097- PRO1107-, PRO1111-, PRO1153-, PRO1182-, PRO1184-, PRO1187-, PRO1281-, PRO23-, PRO39-, PRO834- PRO1317-, PRO1710-, PRO2094-, PRO2145- or PRO2198-encoding genes are amplified in the genome of certain human lung, colon and/or breast cancers and/or cell lines. Amplification is associated with overexpression of the gene product, indicating that the polypeptides are useful targets for therapeutic intervention in certain cancers such as colon, lung, breast and other cancers. Therapeutic agents may take the form of antagonists of PRO212, PRO290, PRO341, PRO535, PRO619, PRO717, PRO809, PRO830, PRO848, PRO943, PRO1005, PRO1009, PRO1025, PRO1030, PRO1097, PRO1107, PRO1111, PRO1153, PRO1182, PRO1184, PRO1187, PRO1281, PRO23, PRO39, PRO834, PRO1317, PRO1710, PRO2094, PRO2145 or PRO2198 polypeptide, for example, murine-human chimeric, humanized or human antibodies against a PRO212, PRO290, PRO341, PRO535, PRO619, PRO717, PRO809, PRO830, PRO848, PRO943, PRO1005, PRO1009, PRO1025, PRO1030, PRO1097, PRO1107, PRO1111, PRO1153, PRO1182, PRO1184, PRO1187, PRO1281, PRO23, PRO39, PRO834, PRO1317, PRO1710, PRO2094, PRO2145 or PRO2198 polypeptide.

The starting material for the screen was genomic DNA isolated from a variety cancers. The DNA is quantitated precisely, *e.g.*, fluorometrically. As a negative control, DNA was isolated from the cells of ten normal healthy individuals which was pooled and used as assay controls for the gene copy in healthy individuals (not shown). The 5' nuclease assay (for example, TaqMan™) and real-time quantitative PCR (for example, ABI Prizm 7700 Sequence Detection System™ (Perkin Elmer, Applied Biosystems Division, Foster City, CA)), were used to find genes potentially amplified in certain cancers. The results were used to determine whether the DNA encoding PRO212, PRO290, PRO341, PRO535, PRO619, PRO717, PRO809, PRO830, PRO848, PRO943, PRO1005, PRO1009, PRO1025, PRO1030, PRO1097, PRO1107, PRO1111, PRO1153, PRO1182, PRO1184, PRO1187, PRO1281, PRO23, PRO39, PRO834, PRO1317, PRO1710, PRO2094, PRO2145 or PRO2198 is over-represented in any of the primary lung or colon cancers or cancer cell lines or breast cancer cell lines that were screened. The primary lung cancers were obtained from individuals with tumors of the type and stage as indicated in Table 2. An explanation of the abbreviations used for the designation of the primary tumors listed in Table 2 and the primary tumors and cell lines referred to throughout this example has been given hereinbefore.

The results of the Taqman™ are reported in delta (Δ) Ct units. One unit corresponds to 1 PCR cycle or

approximately a 2-fold amplification relative to normal, two units corresponds to 4-fold, 3 units to 8-fold amplification and so on. Quantitation was obtained using primers and a Taqman™ fluorescent probe derived from the PRO212-, PRO290-, PRO341-, PRO535-, PRO619-, PRO717-, PRO809-, PRO830-, PRO848-, PRO943-, PRO1005-, PRO1009-, PRO1025-, PRO1030-, PRO1097-, PRO1107-, PRO1111-, PRO1153-, PRO1182-, PRO1184-, PRO1187-, PRO1281-, PRO23-, PRO39-, PRO834-, PRO1317-, PRO1710-, PRO2094-, PRO2145- or PRO2198-encoding gene. Regions of PRO212, PRO290, PRO341, PRO535, PRO619, PRO717, PRO809, PRO830, PRO848, PRO943, PRO1005, PRO1009, PRO1025, PRO1030, PRO1097, PRO1107, PRO1111, PRO1153, PRO1182, PRO1184, PRO1187, PRO1281, PRO23, PRO39, PRO834, PRO1317, PRO1710, PRO2094, PRO2145 or PRO2198 which are most likely to contain unique nucleic acid sequences and which are least likely to have spliced out introns are preferred for the primer and probe derivation, *e.g.*, 3-untranslated regions. The sequences for the primers and probes (forward, reverse and probe) used for the PRO212, PRO290, PRO341, PRO535, PRO619, PRO717, PRO809, PRO830, PRO848, PRO943, PRO1005, PRO1009, PRO1025, PRO1030, PRO1097, PRO1107, PRO1111, PRO1153, PRO1182, PRO1184, PRO1187, PRO1281, PRO23, PRO39, PRO834, PRO1317, PRO1710, PRO2094, PRO2145 or PRO2198 gene amplification analysis were as follows:

PRO212 (DNA30942-1134)

30942.3unt-probe:

5'-CCCTGTGCACTGATCCTGGCCC-3' (SEQ ID NO:80)

30942.3unt-5:

5'-AGCGGAGCGTCCGTGA-3' (SEQ ID NO:81)

30942.3unt-3:

5'-CCACTTGCACTGAAAGAGGCT-3' (SEQ ID NO:82)

30942.tm.p2:

5'-ACACGATGCGTGCTCCAAGCAGAA-3' (SEQ ID NO:83)

30942.tm.f2:

5'-CTTCTTCGCGCACGCTG-3' (SEQ ID NO:84)

30942.tm.r2:

5'-ATCACGCCGGCACCAG-3' (SEQ ID NO:85)

30942.dom1.f3

5'-ACGCGGAGTGGCAGAAAC-3' (SEQ ID NO:86)

30942.dom1.r3:

5'-CACTGGGCGCACACCA-3' (SEQ ID NO:87)

30942.dom1.p3:

5'-TACCCCTGGCGGGACGCAGAG-3' (SEQ ID NO:88)

30942.dom4a.f4:

5'-CACCTTCTCAGCCAGCAGCT-3' (SEQ ID NO:89)

30942.dom4a.r4:

5'-GAGGAAGAGCCTGGCACATT-3' (SEQ ID NO:90)

"Percent (%) nucleic acid sequence identity" with respect to PRO-encoding nucleic acid sequences identified herein is defined as the percentage of nucleotides in a candidate sequence that are identical with the nucleotides in the PRO nucleic acid sequence of interest, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity. Alignment for purposes of determining percent nucleic acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as BLAST, BLAST-2, ALIGN or Megalign (DNASTAR) software. For purposes herein, however, % nucleic acid sequence identity values are generated using the sequence comparison computer program ALIGN-2, wherein the complete source code for the ALIGN-2 program is provided in Table 1 below. The ALIGN-2 sequence comparison computer program was authored by Genentech, Inc. and the source code shown in Table 1 below has been filed with user documentation in the U.S. Copyright Office, Washington D.C., 20559, where it is registered under U.S. Copyright Registration No. TXU510087. The ALIGN-2 program is publicly available through Genentech, Inc., South San Francisco, California or may be compiled from the source code provided in Table 1 below. The ALIGN-2 program should be compiled for use on a UNIX operating system, preferably digital UNIX V4.0D. All sequence comparison parameters are set by the ALIGN-2 program and do not vary.

In situations where ALIGN-2 is employed for nucleic acid sequence comparisons, the % nucleic acid sequence identity of a given nucleic acid sequence C to, with, or against a given nucleic acid sequence D (which can alternatively be phrased as a given nucleic acid sequence C that has or comprises a certain % nucleic acid sequence identity to, with, or against a given nucleic acid sequence D) is calculated as follows:

100 times the fraction W/Z

where W is the number of nucleotides scored as identical matches by the sequence alignment program ALIGN-2 in that program's alignment of C and D, and where Z is the total number of nucleotides in D. It will be appreciated that where the length of nucleic acid sequence C is not equal to the length of nucleic acid sequence D, the % nucleic acid sequence identity of C to D will not equal the % nucleic acid sequence identity of D to C. As examples of % nucleic acid sequence identity calculations, Tables 4 and 5, demonstrate how to calculate the % nucleic acid sequence identity of the nucleic acid sequence designated "Comparison DNA" to the nucleic acid sequence designated "PRO-DNA", wherein "PRO-DNA" represents a hypothetical PRO-encoding nucleic acid sequence of interest, "Comparison DNA" represents the nucleotide sequence of a nucleic acid molecule against which the "PRO-DNA" nucleic acid molecule of interest is being compared, and "N", "L" and "V" each represent different hypothetical nucleotides.

Unless specifically stated otherwise, all % nucleic acid sequence identity values used herein are obtained as described in the immediately preceding paragraph using the ALIGN-2 computer program. However, % nucleic acid sequence identity values may also be obtained as described below by using the WU-BLAST-2 computer program (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Most of the WU-BLAST-2 search parameters are set to the default values. Those not set to default values, i.e., the adjustable parameters, are set with the following values: overlap span = 1, overlap fraction = 0.125, word threshold

(T) = 11, and scoring matrix = BLOSUM62. When WU-BLAST-2 is employed, a % nucleic acid sequence identity value is determined by dividing (a) the number of matching identical nucleotides between the nucleic acid sequence of the PRO polypeptide-encoding nucleic acid molecule of interest having a sequence derived from the native sequence PRO polypeptide-encoding nucleic acid and the comparison nucleic acid molecule of interest (i.e., the sequence against which the PRO polypeptide-encoding nucleic acid molecule of interest is being compared which may be a variant PRO polynucleotide) as determined by WU-BLAST-2 by (b) the total number of nucleotides of the PRO polypeptide-encoding nucleic acid molecule of interest. For example, in the statement "an isolated nucleic acid molecule comprising a nucleic acid sequence A which has or having at least 80% nucleic acid sequence identity to the nucleic acid sequence B", the nucleic acid sequence A is the comparison nucleic acid molecule of interest and the nucleic acid sequence B is the nucleic acid sequence of the PRO polypeptide-encoding nucleic acid molecule of interest.

Percent nucleic acid sequence identity may also be determined using the sequence comparison program NCBI-BLAST2 (Altschul et al., Nucleic Acids Res. 25:3389-3402 (1997)). The NCBI-BLAST2 sequence comparison program may be downloaded from http://www.ncbi.nlm.nih.gov. NCBI-BLAST2 uses several search parameters, wherein all of those search parameters are set to default values including, for example, unmask = yes, strand = all, expected occurrences = 10, minimum low complexity length = 15/5, multi-pass e-value = 0.01, constant for multi-pass = 25, dropoff for final gapped alignment = 25 and scoring matrix = BLOSUM62.

In situations where NCBI-BLAST2 is employed for sequence comparisons, the % nucleic acid sequence identity of a given nucleic acid sequence C to, with, or against a given nucleic acid sequence D (which can alternatively be phrased as a given nucleic acid sequence C that has or comprises a certain % nucleic acid sequence identity to, with, or against a given nucleic acid sequence D) is calculated as follows:

100 times the fraction W/Z

where W is the number of nucleotides scored as identical matches by the sequence alignment program NCBI-BLAST2 in that program's alignment of C and D, and where Z is the total number of nucleotides in D. It will be appreciated that where the length of nucleic acid sequence C is not equal to the length of nucleic acid sequence D, the % nucleic acid sequence identity of C to D will not equal the % nucleic acid sequence identity of D to C.

In other embodiments, PRO variant polynucleotides are nucleic acid molecules that encode an active PRO polypeptide and which are capable of hybridizing, preferably under stringent hybridization and wash conditions, to nucleotide sequences encoding a full-length PRO polypeptide as disclosed herein. PRO variant polypeptides may be those that are encoded by a PRO variant polynucleotide.

The term "positives", in the context of sequence comparison performed as described above, includes residues in the sequences compared that are not identical but have similar properties (e.g. as a result of conservative substitutions, see Table 6 below). For purposes herein, the % value of positives is determined by dividing (a) the number of amino acid residues scoring a positive value between the PRO polypeptide amino

acid sequence of interest having a sequence derived from the native PRO polypeptide sequence and the comparison amino acid sequence of interest (i.e., the amino acid sequence against which the PRO polypeptide sequence is being compared) as determined in the BLOSUM62 matrix of WU-BLAST-2 by (b) the total number of amino acid residues of the PRO polypeptide of interest.

Unless specifically stated otherwise, the % value of positives is calculated as described in the immediately preceding paragraph. However, in the context of the amino acid sequence identity comparisons performed as described for ALIGN-2 and NCBI-BLAST-2 above, includes amino acid residues in the sequences compared that are not only identical, but also those that have similar properties. Amino acid residues that score a positive value to an amino acid residue of interest are those that are either identical to the amino acid residue of interest or are a preferred substitution (as defined in Table 6 below) of the amino acid residue of interest.

For amino acid sequence comparisons using ALIGN-2 or NCBI-BLAST2, the % value of positives of a given amino acid sequence A to, with, or against a given amino acid sequence B (which can alternatively be phrased as a given amino acid sequence A that has or comprises a certain % positives to, with, or against a given amino acid sequence B) is calculated as follows:

100 times the fraction X/Y

where X is the number of amino acid residues scoring a positive value as defined above by the sequence alignment program ALIGN-2 or NCBI-BLAST2 in that program's alignment of A and B, and where Y is the total number of amino acid residues in B. It will be appreciated that where the length of amino acid sequence A is not equal to the length of amino acid sequence B, the % positives of A to B will not equal the % positives of B to A.

"Isolated," when used to describe the various polypeptides disclosed herein, means polypeptide that has been identified and separated and/or recovered from a component of its natural environment. Contaminant components of its natural environment are materials that would typically interfere with diagnostic or therapeutic uses for the polypeptide, and may include enzymes, hormones, and other proteinaceous or non-proteinaceous solutes. In preferred embodiments, the polypeptide will be purified (1) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator, or (2) to homogeneity by SDS-PAGE under non-reducing or reducing conditions using Coomassie blue or, preferably, silver stain. Isolated polypeptide includes polypeptide *in situ* within recombinant cells, since at least one component of the PRO polypeptide natural environment will not be present. Ordinarily, however, isolated polypeptide will be prepared by at least one purification step.

An "isolated" PRO polypeptide-encoding nucleic acid or other polypeptide-encoding nucleic acid is a nucleic acid molecule that is identified and separated from at least one contaminant nucleic acid molecule with which it is ordinarily associated in the natural source of the polypeptide-encoding nucleic acid. An isolated polypeptide-encoding nucleic acid molecule is other than in the form or setting in which it is found in nature. Isolated polypeptide-encoding nucleic acid molecules therefore are distinguished from the specific polypeptide-

encoding nucleic acid molecule as it exists in natural cells. However, an isolated polypeptide-encoding nucleic acid molecule includes polypeptide-encoding nucleic acid molecules contained in cells that ordinarily express the polypeptide where, for example, the nucleic acid molecule is in a chromosomal location different from that of natural cells.

The term "control sequences" refers to DNA sequences necessary for the expression of an operably linked coding sequence in a particular host organism. The control sequences that are suitable for prokaryotes, for example, include a promoter, optionally an operator sequence, and a ribosome binding site. Eukaryotic cells are known to utilize promoters, polyadenylation signals, and enhancers.

Nucleic acid is "operably linked" when it is placed into a functional relationship with another nucleic acid sequence. For example, DNA for a presequence or secretory leader is operably linked to DNA for a polypeptide if it is expressed as a preprotein that participates in the secretion of the polypeptide; a promoter or enhancer is operably linked to a coding sequence if it affects the transcription of the sequence; or a ribosome binding site is operably linked to a coding sequence if it is positioned so as to facilitate translation. Generally, "operably linked" means that the DNA sequences being linked are contiguous, and, in the case of a secretory leader, contiguous and in reading phase. However, enhancers do not have to be contiguous. Linking is accomplished by ligation at convenient restriction sites. If such sites do not exist, the synthetic oligonucleotide adaptors or linkers are used in accordance with conventional practice.

The term "antibody" is used in the broadest sense and specifically covers, for example, single anti-PRO monoclonal antibodies (including agonist, antagonist, and neutralizing antibodies), anti-PRO antibody compositions with polyepitopic specificity, single chain anti-PRO antibodies, and fragments of anti-PRO antibodies (see below). The term "monoclonal antibody" as used herein refers to an antibody obtained from a population of substantially homogeneous antibodies, i.e., the individual antibodies comprising the population are identical except for possible naturally-occurring mutations that may be present in minor amounts.

"Stringency" of hybridization reactions is readily determinable by one of ordinary skill in the art, and generally is an empirical calculation dependent upon probe length, washing temperature, and salt concentration. In general, longer probes require higher temperatures for proper annealing, while shorter probes need lower temperatures. Hybridization generally depends on the ability of denatured DNA to reanneal when complementary strands are present in an environment below their melting temperature. The higher the degree of desired homology between the probe and hybridizable sequence, the higher the relative temperature which can be used. As a result, it follows that higher relative temperatures would tend to make the reaction conditions more stringent, while lower temperatures less so. For additional details and explanation of stringency of hybridization reactions, see Ausubel et al., Current Protocols in Molecular Biology, Wiley Interscience Publishers, (1995).

"Stringent conditions" or "high stringency conditions", as defined herein, may be identified by those that: (1) employ low ionic strength and high temperature for washing, for example 0.015 M sodium chloride/0.0015 M sodium citrate/0.1% sodium dodecyl sulfate at 50°C; (2) employ during hybridization a denaturing agent, such as formamide, for example, 50% (v/v) formamide with 0.1% bovine serum albumin/0.1% Ficoll/0.1% polyvinylpyrrolidone/50mM sodium phosphate buffer at pH 6.5 with 750 mM

Table 2

PRO	XXXXXXXXXXXXXXX	(Length = 15 amino acids)
Comparison Protein	XXXXXYYYYYYY	(Length = 12 amino acids)

% amino acid sequence identity =

(the number of identically matching amino acid residues between the two polypeptide sequences as determined by ALIGN-2) divided by (the total number of amino acid residues of the PRO polypeptide) =

5 divided by 15 = 33.3%

Table 3

PRO	XXXXXXXXXX	(Length = 10 amino acids)
Comparison Protein	XXXXXYYYYYYZZYZ	(Length = 15 amino acids)

% amino acid sequence identity =

(the number of identically matching amino acid residues between the two polypeptide sequences as determined by ALIGN-2) divided by (the total number of amino acid residues of the PRO polypeptide) =

5 divided by 10 = 50%

Table 4

PRO-DNA	NNNNNNNNNNNNNN	(Length = 14 nucleotides)
Comparison DNA	NNNNNNLLLLLLLLLL	(Length = 16 nucleotides)

% nucleic acid sequence identity =

(the number of identically matching nucleotides between the two nucleic acid sequences as determined by ALIGN-2) divided by (the total number of nucleotides of the PRO-DNA nucleic acid sequence) =

6 divided by 14 = 42.9%

Table 5

PRO-DNA	NNNNNNNNNNNN	(Length = 12 nucleotides)
Comparison DNA	NNNNLLLVV	(Length = 9 nucleotides)

% nucleic acid sequence identity =

(the number of identically matching nucleotides between the two nucleic acid sequences as determined by ALIGN-2) divided by (the total number of nucleotides of the PRO-DNA nucleic acid sequence) =

4 divided by 12 = 33.3%